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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SALVOZA, M FRANCO G	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,421	SHYAMALA, VENKATAKRISHNA	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-11, 30-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/05/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/04, 1/26/04*. 12/23/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (claims 12-29) in the reply filed on June 6, 2005 is acknowledged. Applicants elected the sense primer of SEQ ID NO: 34, the antisense primer of SEQ ID NO: 35, the capture oligonucleotide of SEQ ID NO: 8, the probe of SEQ ID NO: 52, and the internal control of SEQ ID NO: 40.

The traversal is on the ground(s) that the capture oligonucleotides can be used alone or in combination, and the use of multiple capture oligonucleotides increases capture efficiency.

Applicant's arguments are considered and found persuasive as to specific sequences. SEQ ID NO: 53 is rejoined since it can be used with SEQ ID NO: 52 when sense primer comprises the sequence of SEQ ID NO: 34. SEQ ID NO: 45 is rejoined to use as an additional capture nucleotide to increase capture efficiency. However, the other nucleotide sequences are structurally distinct chemical compounds deemed to constitute independent and distinct inventions due to structural divergence in sequence and functional divergence for encoding different products, subject to a restriction requirement pursuant to 35 U.S.C. § 121 and 37 CFR 1.141 et seq. (MPEP § 803.04).

Claims 12-29 are pending and under consideration.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on p. 13. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 20 and 21 recite the use of the trademarked term TaqMan. It should be capitalized or accompanied by the ™ or ® symbol wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Additionally, the trademark cannot be used to identify a material, only a source of material.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for detecting WNV in a sample comprising the sense primer comprising SEQ ID NO: 34 or a nucleotide sequence having at least 90% sequence identity thereto; the antisense primer comprising SEQ ID NO:35 or a nucleotide having at least 90% sequence identity thereto. The claims do not require that the primers possesses any particular distinguishing feature, biologic activity, or conserved structure. Therefore, the claims are drawn to a genus of primers that are defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of primers, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only primers comprising the nucleotide sequences set forth in SEQ ID NO:s 34 and 35, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 17, 20-25 are rejected under 103(a) over Lanciotti et al. (2000) (hereinafter, "Lanciotti 1") and Lanciotti et al. (1999) (hereinafter, "Lanciotti 2") in view of Buck et al. ("Design strategies and performance of custom DNA sequencing primers" (Biotechniques (1999) 27(3): 528-536)).

Claim 12 recites a method for detecting the presence of West Nile virus in a sample comprising isolating nucleic acids from a biological sample, amplifying the nucleic acids using a sense and an antisense primer wherein each of the primers is not more than 60 nucleotides in length and is sufficiently complementary to a portion of the sense and antisense strands, respectively, of the isolated nucleic acid to hybridize therewith, and the sense primer comprises SEQ ID NO: 34 or a nucleotide having at least 90% sequence identity thereto; the antisense primer comprises SEQ ID NO: 35 or a nucleotide sequence having at least 90% sequence identity thereto when the sense primer is SEQ ID NO: 34, and detecting the presence of the amplified nucleic acids as an indication of the presence of WNV in the sample.

Claim 17 further recites the method wherein the capture nucleic acids comprise one or more nucleotides in length and comprises SEQ ID NO:s 8 and 45.

Claim 20 recites the method of claim 12, wherein amplifying comprises RT-PCR, transcription mediated amplification (TMA) or TaqMan, or a combination thereof; claim 21 recites wherein amplifying comprises TaqMan using sense primer and the antisense primer detecting is done using at least one probe comprising a detectable label.

Claims 22 and 23 recite the method of claim 21 wherein the at least one probe is not more than 60 nucleotides in length and comprises the sequence of SEQ ID NO: 52 or the sequence of SEQ ID NO: 53 when the sense primer comprises the sequence of SEQ ID NO: 34. Claim 24 recites wherein the probe further comprises detectable labels at the 5' end and at the 3' end. Claim 25 recites wherein the detectable label is a fluorescent label selected from the group consisting of 6-FAM, TAMRA and TET.

Lanciotti 1 teaches a method of amplifying and detecting WNV in a sample using a

TaqMan assay (p. 4066) and RT-PCR assay. Lanciotti 1 also teaches isolation and amplification using primers (p. 4067). Lanciotti 1 further teaches detection through the use of probes labeled at the 5' end and at the 3' end using FAM reporter dye and TAMRA (p. 4067).

Lanciotti 1 does not teach specifically SEQ ID NO:s 8, 17, 34, 35, 40, 45, 52, 53.

Lanciotti 2 teaches the complete nucleotide sequence of one of the viral isolates of the WNV genome (p. 2334). Buck et al. (Biotechniques (1999) 27(3):528-536) teaches the use of primers and combinations of primers for use in assays.

One of ordinary skill in the art would have been motivated combine the TaqMan and RT-PCR methods of Lanciotti 1 with sequences from the WNV genome to construct primers to detect WNV sequences in a sample from Lanciotti 2.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs of the oligonucleotides taught by Lanciotti 2, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of the primers, MPEP 2144.06 notes "Substituting equivalents known for the same purpose. In order to rely on equivalence as a

rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

With regard to the issue of reasonable expectation of success in using such equivalents, Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Therefore, the invention as a whole would have been prima facie obvious to one of

ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 12-17, 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanciotti 1 and Lanciotti 2 in view of Buck et al. and further in view of Bhatt et al. ("Detection of Nucleic Acids by Cycling Probe Technology on Magnetic Particles; High Sensitivity and Ease of Separation," Nucleosides Nucleotides, 18(6-7): 1297-9 (1999)).

Claim 12 recites a method for detecting the presence of West Nile virus in a biological sample, comprising isolating nucleic acids from a biological sample suspected of containing the WNV, amplifying the nucleic acids using a sense and an antisense primer, and detecting the presence of the amplified nucleic acids as an indication of the presence of WNV in the sample.

Claim 13 recites the isolation step of the method, wherein the nucleic acids are isolated from the biological sample by a method comprising contacting a solid support comprising capture nucleic acids associated therewith with a biological sample under hybridizing conditions wherein nucleic acid strands, if present in the biological sample, hybridize with the capture nucleic acids; and separating the solid support from the sample. Claim 14 further recites wherein the solid support comprises beads, and claim 15 further recites wherein the beads are magnetic beads.

Claim 16 also recites wherein the isolating, amplifying and detecting are performed in a single container.

(See the recitations for the pursuant claims above.)

See the teachings of Lanciotti 1 and Lanciotti 2 in view of Buck et al. above. Lanciotti 1

and Lanciotti 2 in view of Buck et al. do not teach a method comprising isolating nucleic acids from a biological sample and contacting a solid support comprising capture nucleic acids and magnetic beads for hybridization purposes.

Bhatt et al. teaches a solid support with magnetic beads and capture nucleic acids attached for hybridization to complementary target nucleic acid sequences in a biological sample (p. 1297). Bhatt et al. also does not teach the use of separate containers for the method steps.

One of ordinary skill in the art at the time the invention was made would have had a motivation to combine the TaqMan/RT-PCR methods of amplification and detection of Lanciotti 1 and Lanciotti 2 in view of Buck et al. with the isolation step of Bhatt et al. because Bhatt et al. teaches that capturing the target DNA on particles and separating it from non-specific DNA dramatically reduces background for enhanced specificity (p. 1297).

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the isolating step of Bhatt et al. with the amplification and detection step of Lanciotti 1 and Lanciotti 2 in view of Buck et al. because both teach the detection of nucleic acids in a sample using capture nucleic acids, primers and labeled probes.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Lanciotti 1 and Lanciotti 2 in view of Buck et al. and Bhatt et al. and further in view of Suzuki et al. ("Poly A-linked non-isotopic microtiter plate reverse transcriptase assay for detection of clinical human immunodeficiency virus isolates," Journal of Virological Methods, 55: 347-356 (1995)).

Claim 18 recites the method of claim 17 wherein the capture nucleic acids further comprise a homopolymer chain of about 10-25 nucleotides in length selected from the group consisting of polyA, polyT, polyG, polyC and polyU. Claim 19 recites the homopolymer chain of polyA.

See the teachings of Lanciotti 1 and Lanciotti 2 in view of Buck et al. and Bhatt et al. above. Lanciotti 1 and Lanciotti 2 in view of Buck et al.and Bhatt et al. do not explicitly teach the use of the capture nucleic acids further comprising a homopolymer chain consisting of polyA.

Suzuki et al. teaches a reverse transcriptase assay for virus detection incorporating labeled dUTP onto oligo-dT primers that are hybridized to polyA templates. (p. 347)

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the TaqMan/RT-PCR methods of amplification and detection of Lanciotti 1 and Lanciotti 2 in view of Buck et al. with the poly-A chains of Suzuki et al. because Suzuki et al. teaches that attaching oligonucleotide primers to polyA templates increased the efficiency of capture of the labeled nucleotide compared to the solution phase format and eliminated a transfer step to improve use and assay reproducibility (p. 355).

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the polyA template of Suzuki et al. with the

amplification and detection step of Lanciotti 1 and Lanciotti 2 in view of Buck et al. because both teach the detection of nucleic acids in a sample using capture nucleic acids, primers and labeled probes.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanciotti 1 and Lanciotti 2 in view of Buck et al and Bhatt et. al. and Suzuki et al. further in view of King et al. ("Development of a Taqman PCR assay with internal amplification control for the detection of African swine fever virus," Journal of Virological Methods, 107: 53-61 (2003)).

Claims 26-29 recite the method of claim 12 wherein an internal control sequence is present comprising the nucleotide sequence SEQ ID NO:17 as well as a detectably labeled probe sequence.

See the teachings of Lanciotti 1 and Lanciotti 2 in view of Buck et al., Bhatt et al. and Suzuki et al. above. Lanciotti 1 and Lanciotti 2 in view of Buck et al., Bhatt et al. and Suzuki et al. do not explicitly teach the use of an internal control sequence.

King et al. teaches a TaqMan assay for African swine fever virus detection incorporating an internal control plasmid. (p. 2636)

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the TaqMan/RT-PCR methods of amplification and detection of Lanciotti 1 and Lanciotti 2 in view of Buck et al., Bhatt et al. and Suzuki et al. with the internal control sequence of King et al. because King et al. teaches the use of an internal control sequence to use

as a positive control for the reverse transcription or amplification steps (p. 54). King also teaches the use of detectably labeled probes (p.57).

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the internal control sequence of King et al. with the amplification and detection step of Lanciotti 1 and Lanciotti 2 in view of Buck et al., Bhatt et al and Suzuki et al. because both teach the detection of viral nucleic acids in a sample using capture nucleic acids, primers and labeled probes.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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1/23/06

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